Practitioner's Docket No. MPI96-031CP1DV1CPACN2M **U.S.S.N. 10/810,793**

REMARKS

The present Amendment and the following Remarks are submitted in response to the Office Communication mailed February 12, 2007. Applicant thanks the Examiner for entering the previous amendment to the claims and for indicating that the previous rejections are withdrawn.

The specification is being amended to designate SEQ ID NOs and to designate trademarks.

Claims 10 and 18 are being amended. Support for the amendment to claim 18 can be found in the specification at, for example, page 72, lines 9-19. Claims 7-8 and 10-19 are pending upon entry of these amendments.

No new matter is being added. The Objections and Rejections raised by the Examiner in the Communication are addressed below.

Paragraphs 4 and 5. Objections to the Specification

An objection to the disclosure arose from the absence of SEQ ID NOs when referring to sequences. In response, Applicant is adding SEQ ID NOs for sequences included in the Sequence Listing.

A second objection to the disclosure arose from the use of trademarks in the specification. In response, Applicant is designating trademarks by amendment herein.

In view of these amendments, withdrawal of these objections is respectfully requested.

Paragraph 6. Objection to the Claims

An objection to claim 10 arose due to apparent redundancy of a claim term. In response, Applicant is amending this claim to remove the redundancy. In view of this amendment, withdrawal of thisobjection is respectfully requested

Paragraph 8. Rejection of the Claims Under 35 U.S.C. §112, First Paragraph

Claims 18 and 19 were rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Specifically, the rejection centers on the use of the generic term "binding partner." This term appears to have been misunderstood by the Examiner. Herein, Applicant amends claim 18 to clarify the language. The specification refers to methods of detection at page 71 and describes labeled reagents for detection at page 72, further supplemented by the disclosure at page 69, line 27-page 70, line 7. One of skill in the art has considerable experience with antibody detection reagents

and methods and can use the kit recited in claims 18 and 19 without undue experimentation. In view of this amendment and these remarks, Applicant respectfully requests withdrawal of this rejection.

Paragraph 9. Rejection of the Claims Under 35 U.S.C. §112, First Paragraph

Claims 7-8 and 10-19 were rejected under 35 U.S.C. §112, first paragraph on the grounds that the specification does not contain an adequate written description of the claimed invention and does not reasonably convey to one skilled in the art that the inventor had possession of the claimed invention at the time the application was filed. In particular, the Examiner alleges that Applicant was "not in possession of an antibody or an antigen-binding fragment thereof which binds specifically to a generically recited "a kinase or a subunit thereof," wherein the kinase is defined solely by its ability to phosphorylate IkBa and by approximate molecular weight." Applicant respectfully traverses this rejection.

The Examiner first comments that Applicant is "only in possession of" an antibody or antigen-binding fragment thereof which binds specifically to kinase as recited in the claims with the additional recitation of "ubiquitin dependent." However, Applicant respectfully reminds the Examiner that this kinase does not necessarily require ubiquitin to work and that the specification discloses multiple activators of the kinase and activity without activation (e.g., at page 6, lines 15-17, page 35, line 11, page 36, line 6).

The Examiner supports this rejection by referring to literature that discloses many different kinases can phosphorylate IκBα and that there is extensive structural variability among kinases. The Examiner further alleges that there are only limited identifying characteristics of the recited kinase which are insufficient to show possession together with the ability to phosphorylate IκBα and approximate molecular weight. The Examiner appears to consider the claims to recite a genus which is only limited by the term "kinase" and the general ability to phosphorylate IκBα. The Examiner acknowledged that the Written Description Requirement may be met by actual reduction to practice of a representative number of species, disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such characteristics. Applicant submits that the combination of features disclosed by Applicant shows possession of the claimed invention as explained below.

The first aspect to consider is the recited, disclosed and exemplified activity, namely phosphorylation of IκBα at serine residues 32 and 36. As explained in the Background, page 4, line 26-page 5, line 12, wherein many of the Examiner's references are discussed, the ability to phosphorylate IκBα at the recited residues is unique to the kinase disclosed in the present application. For example, the Kuno et al. reference noted phosphorylation of IκBα at serine-293, the Barroga et al. noted

phosphorylation at the C-terminus and further described candidate residues as serines and threonines 283, 288, 291, 293 and 296. Furthermore, at page 34, line 16-page 35, line 10 of the specification, Applicant contrasts the activity of the kinase disclosed in the application from the activity disclosed in references cited by the Examiner. Applicant additionally provides evidence (Fig. 15A and page 43, lines4-8) that the kinases in the references phosphorylate different regions of IκBα than the kinase complex in the present application.

The second aspect to consider is the recited, disclosed and exemplified approximate molecular weight. None of the kinases in the articles cited by the Examiner is a complex of approximately 700 kDa. For Example, Diaz-Meco et al describes a 50 kDa protein as the kinase responsible for the IκBα phosphorylation (page 2846, col. 1); Kuno et al. describes a 42 kDa kinase for the activity (page 27918, col. 2); Kumar et al describe PKR as p68, a terminology which indicates the kinase is about 68 kDa (abstract); and Barroga used casein kinase II (a tetramer of about 150 kDa) with a catalytic subunit of 44 kDa (legend of Fig 2).

The previous two paragraphs demonstrate that Applicant has described a kinase complex with a unique function readily recognizable to those skilled in the art and a unique structure as a complex readily recognizable to those skilled in the art. Furthermore, the specification provides additional identifying features which show possession of the claimed invention. For example, the specification discloses that the complex comprises a number of subunits, which are identified by molecular weights, p85, p70, p62, p55, p50, p43, p40, p38, p36, p33, and p31 (see, e.g., page 14, lines 4-11). This disclosure further indicates that the p85 subunit is effecting the observed phosphorylation of IκBα for further correlation of structure with the function of the complex. In addition, the specification discloses some sequences (peptide and nucleic acid) of contributors to the complex Figs. 21, 22). Furthermore, Applicant determines the Km of the kinase (Example 19, page 107) and demonstrates an inhibition profile using inhibitors of the kinase activity (Example 24, page 112 and Fig. 24).

Another aspect for satisfying the written description requirement is the disclosure of a representative number of species. In this regard, Applicant provides disclosure of more than one species, but limited variation within the genus. For example, Figs. 14A and B show that the MEKK1- and ubiquitin- induced approximately 700 kDa kinases which phosphorylates IκBα at serines 32 and 36 are indistinguishable by several steps of fractionation. However, upon additional inspection in another fractionation step, species are identifiable through their stimulation means (page 42, lines 5-22). This disclosure demonstrates that Applicant was in possession of a representative number of species in the genus.

In summary, Applicant has provided a kinase identifiable by a unique function and approximate molecular weight, correlation of structure with function and has reduced to practice a representative

number of species in the claimed genus. Applicant provided this disclosure concurrent with exemplification using methods well-known to those of skill in the art. The recitation of the phosporylation of IκBα at serines 32 and 36 shows possession of a kinase distinct from other kinases and the approximate 700 kDa molecular weight represents a distinct genus of complex which was reduced to practice. One of skill in the art readily would recognize possession of antibodies which specifically recognize this complex. In view of these remarks, the Applicant respectfully requests withdrawal of this rejection.

Paragraph 11. Rejection of the Claims Under 35 U.S.C. §102

Claims 7-8, 10-11 and 13-17 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Yoshitaka et al., as evidenced by Diaz-Meco et al. and Pracht et al.. The basis of this rejection is the disclosure of antibodies to protein kinase C in Yoshitaka et al. As discussed in the response above, Applicant clearly contrasts the activity of the kinase of the present application from protein kinase C. Yoshitaka et al. did not disclose producing antibodies to a kinase which phosphorylates IκBα at serines 32 and 36. In fact, Applicant could not find disclosure in Yoshitaka et al. any mention of IκBα or its alternative name, MAD-3. Furthermore, Diaz-Meco et al. does not disclose that PKCζ is the kinase which phosphorylates IκBα, but rather PKCζ stimulates the activity of a 50 kDa kinase (abstract). That kinase is not identified as PKC. Accordingly, the antibodies disclosed in Yoshitaka et al. do not anticipate the claimed antibodies because the kinase they recognize does not have the recited activity. Withdrawal of the rejection is respectfully requested.

Paragraph 13. Rejection of the Claims Under 35 U.S.C. §103(a)

Claims 7 and 10 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable by Yoshitaka et al., as evidenced by Diaz-Meco et al. and Pracht et al. in view of Kuus-Reichel et al.. The basis of this rejection is the disclosure of antibodies to protein kinase C in Yoshitaka et al., with the evidence of IκBα kinase activity by Diaz-Meco et al. and association with an approximately 700 kDa complex in Pracht et al. and use of antibody fragments in Kuus-Reichel et al.. Applicant respectfully traverses this rejection.

As discussed above, neither Yoshitaka et al. nor Diaz-Meco et al. disclosed a kinase which phosphorylates IκBα at serines 32 and 36. Pracht et al. also does not disclose such activity. Furthermore, the approximately 700 kDa BCR complex disclosed by Pracht et al is membrane-bound (page 1, col.2). The kinase disclosed in the present application is isolated from a cytoplasmic fraction (see e.g., page 88, line19). Thus, Pracht et al. does not evidence association of the kinase against which Yoshitaka et al. raised antibodies in a complex disclosed in the present application. The Kuus-Reichel et al. reference

does not supplement the other three disclosures to make it obvious for one of skill in the art to produce the claimed antibodies. In view of these remarks, Applicant respectfully requests withdrawal of the rejection.

Paragraph 14. Rejection of the Claims Under 35 U.S.C. §103(a)

Claims 7, 11 and 12 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable by Yoshitaka et al., as evidenced by Diaz-Meco et al. and Pracht et al. in view of Campbell et al.. The basis of this rejection is the disclosure of antibodies to protein kinase C in Yoshitaka et al., with the evidence of IκBα kinase activity by Diaz-Meco et al. and association with an approximately 700 kDa complex in Pracht et al. and the general properties of monoclonal antibodies in Campbell et al.. As discussed above, the kinase against which Yoshitaka et al. raised antibodies does not phosphorylate IκBα at serines 32 and 36, Diaz-Meco et al. does not evidence such activity, Pracht et al. does not demonstrate association of Yoshitaka et al.'s kinase with the 700 kDa kinase disclosed in the present application. Furthermore, Campbell et al. does not supplement the Yoshitaka et al. with the activity recited in the claims. In view of these remarks, Applicant respectfully requests withdrawal of the rejection.

Paragraph 15. Rejection of the Claims Under 35 U.S.C. §103(a)

Claims 18 and 19 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable by Yoshitaka et al., as evidenced by Diaz-Meco et al. and Pracht et al. in view of Zuk et al.. The basis of this rejection is the disclosure of antibodies to protein kinase C in Yoshitaka et al., with the evidence of IκBα kinase activity by Diaz-Meco et al. and association with an approximately 700 kDa complex in Pracht et al. and the disclosure of provision of immunoassay reagents in a kit by Zuk et al.. As discussed above, the kinase against which Yoshitaka et al. raised antibodies does not phosphorylate IκBα at serines 32 and 36, Diaz-Meco et al. does not evidence such activity, Pracht et al. does not demonstrate association of Yoshitaka et al.'s kinase with the 700 kDa kinase disclosed in the present application. Furthermore, Zuk et al. does not supplement the Yoshitaka et al. with the activity recited in the claims. In view of these remarks, Applicant respectfully requests withdrawal of the rejection.

CONCLUSION

The foregoing amendments and remarks are being made to place the Application in condition for allowance. Applicant respectfully requests the timely allowance of the pending claims because, in view of these amendments and remarks, Applicant respectfully submits that the objections to the specification and claims and the rejections of the claims under 35 U.S.C. §§ 112, 102 and 103 are overcome. Applicant believes that this application is now in condition for allowance. Early notice to this effect is solicited.

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If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned. If the Examiner disapproves of Applicant's amendments and remarks in this response, Applicant requests a prompt mailing of a notice to that effect.

This paper is being filed timely as a request for a three month extension of time is filed concurrently herewith. No additional extensions of time are required. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

13 August 2007

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